REMARKS

Introduction

With this amendment claims 1-3, 5-12, 15-16 and 18-24 are pending of which claims 1 and 20-22 are independent claims. All of the independent claims have been amended.

The Non-Art Rejections

The Examiner rejected claims 1-3, 5-12, 16, 18, and 19-24 under section 112, first paragraph, of the Patent Code based upon lack of written description for the ranges set forth in the claims. The ranges have been amended and the rejection obviated.

The Examiner rejected claims 5 and 19 under section 112, first paragraph, of the Patent Code based upon indefiniteness in view of the use of the word "derivatives." Reference to derivatives in the claims has been removed and that rejection has been obviated.

The Examiner rejected claim 21 for reference to "balancing." The phrase concerning "balancing" has been removed and that rejection has been obviated.

The Art Rejections

The Examiner rejected claims 1-3, 5, 15 and 16 as anticipated by Kiliaan.

The Examiner rejected claims 1 and 6-12 as obvious based upon Morrison et al. over Haynes.

The Examiner rejected claims 21 and 22-24 as obvious based upon Kiliaan.

The References

1. Kiliaan Does Not Have Both Wax And Fat

The composition disclosed in Example 1 on page 13 of Kiliaan et al. does not disclose the wax component. With respect to the rejections based upon Kiliaan, applicants refer the Examiner's attention to page 6, first full paragraph paragraph of the pending application, where it is stated that the specific combination of fat and wax exhibit particularly advantageous properties in respect of shear dilution. The pending application states:

> Phosphatidyl serine and phosphatidyl choline are in particular stabilized according to the invention by other matrix components which are selected such that the total matrix (i.e. composed of PS/PC and the other components) is solid at room temperature and namely to such an extent that when using fats (triglycerides) the solid proportion of the triglyceride that can be determined by TLC is >80% at 23° C. In addition the components are advantageously selected such that the total matrix exhibits the property of shear dilution which for example can be achieved by the preferred use of a combination of fat and wax (e.g. bee wax) in conjunction with PC/PS in the matrix when the triglyceride contains a sufficiently high proportion of solid i.e. unmelted triglycerides. In this case preferred matrix components have a proportion of saturated fatty acids of more than 50% and advantageously no more than four mainly occurring triglyceride species are present. In this connection the use of palm kernel oil together with bee wax has proven to be particularly advantageous.

(Pg. 6, first full paragraph.)

Further, Kiliaan, such as in Example 1, describes a capsule which includes as active components phosphatidyl serine, phosphatidyl choline, omega fatty acids, and vitamins. The latter blend, however, does not have these ingredients in an amount and ratio that would make any matrix solid or make the blend highly viscous and have shear thinning properties to provide the stability described in the instant above application. See attached declaration of Markl.

Kiliaan el al. do not describe a stable solid matrix. Because the amounts and relative amounts of phosphatidyl serine and fatty acids are lower than what is described in the above instant application, the capsule described in Kiliaan's Example 1 would not be a dosage form which becomes a solid matrix at room temperature, nor would it have the shear thinning as described in the above instant application. See attached declaration of Markl.

Even further, formulating materials with phospholipids, due to the amounts of fatty acids in Kiliaan's Example 1, a stable matrix would not be formed. As a result, Kiliaan's blend of ingredients and relative amounts of ingredients would not provide the properties and stability described and sought in the instant above identified application. Also, Kiliaan's composition of Example 1 contains herbal extracts which would not promote stability of any matrix in Kiliaan's blend. See attached declaration of Markl.

2. Morrison and Haynes Are Both Directed To Coating With Phospholipids And Do Not Describe Using Phosphatidylserine And Phosphatidylcholine Together

Both Morrison and Haynes are directed to coatings and describe coating with phospholipids, not coating or encapsulating the phospholipid as discussed below. In contrast thereto, the current application is concerned with the formulation of phospholipids in an encapsulated matrix that keeps them stable, e.g. for providing them as a master batch in an economically acceptable manner. Thus, the skilled person would not consider coating crystalline drugs with a phospholipid (Haynes) or hydrophobic or hydrophilic drugs (Morrison) when developing an encapsulated matrix formulation that provides encapsulated stable phospholipids, namely phosphatidylserine and phosphatidylcholine.

Secondly, although Morrison et al. disclose in Table VIII (which is mislabeled Table VII), column 18, phosphatidylserine and phosphatidylcholine as representative coating substances, the Table is clear that phosphatidylserine would be used as an anionic coating and phosphatidylcholine would be used as a zwitterionic coating. Morrison et al. do not suggest using phosphatidylserine and phosphatidylcholine simultaneously or together as parts of one coating. In addition, because the serine and choline substances Morrison describes in Table VIII

are used as coatings, these substances are used in small amounts, e.g. 0.1% -0.5% PVP (cf. column 19, lines 47-50 of Morrison et al.). Morrison does not disclose how to formulate larger amounts of phosphatidylserine and phosphatidylcholine as part of a matrix as described in the instant application. Haynes et al. likewise discloses phosphatidylcholine and phosphatidylserine merely as coating substances with the same drawbacks as described for the coatings in Morrison et al. above.

Additionally Haynes et al. teach away from using phosphatidylserine and phosphatidylcholine in combination. Reference to the Haynes et al. specification bridging column 13 and 14 has a discussion of how preference is given to the use of lecithin (phosphatidyl choline) as a class A material over a class B phospholipids due to the high cost of class B phospholipids (the class to which phosphatidyl serine belongs).

Further, the product described in the claims is an encapsulated product that includes both phosphatidylserine and phosphatidylcholine. Mixtures of these phosphatidyl compounds have been difficult to provide in a stable form. As stated in the last paragraph beginning on page 2 and first paragraph on page 3 of the pending application:

> Formulations of phosphatidyl serine and phosphatidyl choline especially in a mixture with other lecithins and/or oils have proven to be not sufficiently stable in soft capsules. Also there are very tight constraints on the mixing (blending) with regard to the melting point and flow behaviour of the capsule contents due to the technical requirements of the encapsulation which is effected typically by means of a so-called rotary dye. Also the processing temperatures in the encapsulation process often have an adverse effect on the properties of the capsule coat and/or the capsule contents.
>
> One result of this described instability of the lecithins as capsule contents is that at best moderately pasty blends can be encapsulated instead of a desired liquid formulation.

Encapsulation phosphatidylserine and phosphatidylcholine without the matrix described in the present application does not provide sufficiently stable capsules due to the

tight constraints on the mixing with regard to the melting point and flow behavior of the capsule contents. In addition, without the matrix as described in the present application, the problem with encapsulated phospholipids is that they also act as emulsifiers which lead to a permeable capsule as the phospholipids mix with the coat. Thus, the advantage of the combination of phosphatidylserine and phosphatidylcholine with the matrix according to the present application allows for a stable formulation of these phospholipids in an encapsulated state. Applicants respectfully refer the Examiner to page 10 of the present application which shows a comparative example of encapsulated phosphatidylserine. Examples 1-3 in Table 1 on page 10 show the stability of encapsulated phosphatidylserine embedded in the matrix of the invention compared to Examples 4-6 which show the standard formulation wherein phosphatidylserine is encapsulated by the standard rotary dye process without the inventive matrix. It can be seen from Table 1 that the capsules in which phosphatidylserine is embedded into the inventive matrix, a higher stability is achieved after 12 months compared to the standard formulation without matrix.

The Commissioner is hereby authorized to charge any additional fees which may be required with respect to this communication, or credit any overpayment, to Deposit Account No. 06-1135.

Respectfully submitted,

FITCH, EVEN, TABIN & FLANNERY

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